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Duration of Ejection in Aortic Stenosis: Effect of Stroke Volume and Pressure Gradient

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The theoretical effect of variable ventricular function on left ventricular ejection time in aortic stenosis was predicted by applying data measured in 52 patients with pure aortic stenosis to equations derived from the relations of Gorlin and Gorlin and Weissler et al. Ejection time and aortic valve area are not, of necessity, linearly related because

$$\text{LVET} = k \frac{\text{SV}}{\sqrt{\text{PG}}} \frac{1}{\text{AVA}},$$

where LVET is left ventricular ejection time, k is a constant, SV is stroke volume, PG is mean aortic pressure gradient and AVA is aortic valve area.

When the patients were separated into performance groups on the basis of cardiac index (at 2.8 liters/min per m^2), the linear regression relating the measured SV/$\sqrt{PG}$ with valve area in 18 patients with normal function (SV/$\sqrt{PG}$ = 11.1 AVA + 2.0, r = 0.969, p < 0.001) predicted ejection time prolongation with decreasing valve area. In 34 patients with poor function, however, the decrease in SV/$\sqrt{PG}$ with decreasing valve area was more marked (SV/$\sqrt{PG}$ = 12.6 AVA + 0.4, r = 0.894, p < 0.001), predicting a shorter ejection time at any given valve area in this group. As predicted by the effect of valve area on the equation, ejection time becomes most variable at a small aortic valve area. Independent ejection time measurement in these patients validated the predicted effect.

Prolongation of left ventricular ejection time is a useful sign of aortic stenosis (1,2) Despite the tendency of ejection time to increase with increasing valvular obstruction, correlation with aortic valve area is poor, so that at any given valve area a wide range of ejection times is found (3–5) Although with additional valve lesions, variation in ejection time duration can be explained by forward stroke volume changes caused by aortic regurgitation, mitral stenosis and mitral regurgitation (4), the mechanism of ejection time variation caused by depressed ventricular performance remains unclear (5)

We propose an analysis of ejection time variability in aortic stenosis that provides insight into the relation of increasing aortic obstruction, decreasing ventricular performance and the duration of ejection From the equation of Gorlin and Gorlin (6)

$$\text{AVA} = \frac{\text{CO/SEP}}{44.5\sqrt{\text{PG}}},$$

where aortic valve area (AVA) is calculated at catheterization from measurement of cardiac output (CO), systolic ejection period (SEP) and aortic valve pressure gradient (PG) The relation of systolic ejection period to ejection time allows rearrangement of terms to demonstrate that

$$\text{LVET} = k \frac{\text{SV}}{\sqrt{\text{PG}}} \frac{1}{\text{AVA}},$$

where LVET is left ventricular ejection time, k is a derived constant, SV is the calculated stroke volume, PG is the mean pullback pressure gradient across the aortic valve and AVA = aortic valve area Rate correction of ejection time can be performed using the regression data of Weissler et al (7,8) (Table 1)

The ejection time equation reveals that, independent of variation in stroke volume and pressure gradient, the relation of ejection time to valve area is not linear Furthermore, it is apparent that at a fixed valve area, the duration of ejection is governed by the relation of stroke volume to the square root of the pressure gradient Accordingly, we have ex-

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Table 1. Equations Used to Calculate Valve Area and Ejection Time

1 Relations of Gorlin and Gorlin (6) for calculation of aortic valve area

$$AVA = \frac{CO/SEP}{k' \sqrt{PG}}$$

2 Derived equation for predicted duration of ejection

$$LVET = k \frac{SV}{\sqrt{PG}} \frac{1}{AVA}$$

3 Relation of Weissler et al (9) for rate correction of predicted ejection time

$$LVETI = LVET + k'' HR$$

AVA = aortic valve area, CO = cardiac output, HR = heart rate, k, k', k'' = constants, LVET = left ventricular ejection time (duration of ejection), LVETI = rate-corrected left ventricular ejection time (index), PG = pressure gradient, SEP = systolic ejection period

amined the hemodynamic changes that accompany increasing aortic valve obstruction to address the following questions 1) Can observed hemodynamic data be used to predict the measured and rate-corrected ejection time in aortic stenosis? 2) How do the hemodynamic determinants of ejection time vary with ventricular performance? 3) Can these data be used to predict and explain the different durations of ejection observed in patients with good and poor ventricular function? 4) Can these data predict and explain increasing scatter of ejection time at smaller valve areas?

Methods

Study group. The cardiac catheterization records and tracings of 100 consecutive adult patients with valvular aortic stenosis and no additional valve lesions were examined Of these 100 patients, 48 were excluded because of coincident intraventricular conduction abnormalities (QRS duration > 100 ms) known to alter the time intervals or because of technically suboptimal pressure tracings for the purposes of this study The study group, therefore, consisted of 52 adult patients with pure valvular aortic stenosis, with a calculated aortic valve area of 0 2 to 1 4 cm^2

Cardiac catheterization. Left heart catheterization was performed via femoral puncture with Sones catheters connected to fluid-filled pressure transducers All pressures reported were obtained within 10 beats of pullback from left ventricle to proximal aortic root Right heart catheterization was performed with Cournand catheters, and cardiac output was calculated from measured oxygen consumption and oxygen contents

Calculation of predicted rate-corrected ejection time curves in relation to ventricular function. Valve area was calculated from the standard Gorlin relation (Table 1) (6) using a constant of 44 5 Pressure gradients were measured by planimetry using an average of three cycles The theoretical determinants of left ventricular ejection time were calculated for individual patients from measured stroke volume and pressure gradient The predicted duration of ejection (in milliseconds) was calculated for each patient according to the derived equation by multiplying the $SV/\sqrt{PG} \cdot 1/AVA$ product by 22 47, the dimensional constant derived from the formula of Gorlin and Gorlin

To assess the effect of ventricular function on the determinants of ejection time, the 52 patients were divided into two subgroups on the basis of a cardiac index partition of 2 8 liters/min per m^2, which is 1 standard deviation below the mean normal value for this laboratory Within each performance subgroup, linear regression equations were calculated to relate stroke volume (SV) pressure gradient (PG) and the $SV/\sqrt{PG}$ ratio to aortic valve area For each performance subgroup, solution of the $SV/\sqrt{PG}$ equation over a wide range of valve areas was substituted in the derived ejection time equation to yield predicted ejection time curves on the basis of ventricular function Rate correction of these predicted ejection times, using mean heart rate data from performance and valve area subgroups, was used to calculate predicted rate-corrected ejection time curves for patients with good and poor ventricular function (7,8)

Comparison of predicted and actual ejection time. The duration of left ventricular ejection was measured in each patient from the onset of upstroke of the central aortic pressure pulse to the incisura according to standard methods (4) This measured left ventricular ejection time was compared with predicted ejection time for all patients The equations used in this study are shown in Table 1

Results

Among 52 patients with pure aortic stenosis, there were 18 with good ventricular function (cardiac index ≥ 2 8 liters/min per m^2) and 34 with poor ventricular function (cardiac index < 2 8 liters/min per m^2) Calculated aortic valve area ranged from 0 2 to 1 4 cm^2

Stroke volume, pressure gradient and aortic valve area in patients with good and poor ventricular performance. For each performance subgroup, a different strong linear correlation was found between the ratio of stroke volume to the square root of pressure gradient and aortic valve area (Fig 1A) For patients with good ventricular function, $SV/\sqrt{PG} = 11.1\ AVA + 2\ 0$ (correlation coefficient [r] = 0 969, probability [p] < 0 001), where SV is stroke volume, PG is pressure gradient, and AVA is aortic valve area For patients with poor ventricular function, $SV/\sqrt{PG} = 12.6\ AVA + 0\ 4$ ($r = 0\ 894$, $p < 0\ 001$) It is apparent in Figure 1A that over the range of smaller valve areas, the ratio of stroke volume to the square root of the pressure gradient is consistently higher in patients with good rather than poor ventricular function

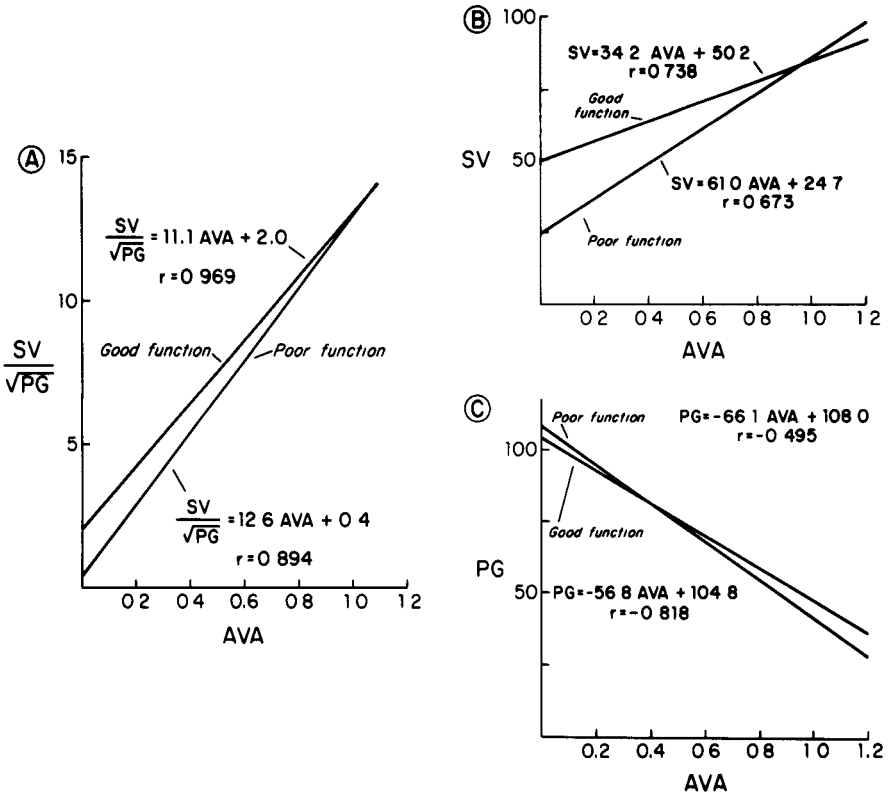


Figure 1. Relation of hemodynamic determinants of ejection time to aortic valve area (AVA) in patients with good and poor left ventricular function At smaller valve areas, the ratio of stroke volume (SV) to the square root of the pressure gradient (PG) is higher among patients with good function (**A**) This is due predominantly to differences in stroke volume (**B**) rather than pressure gradient (**C**)

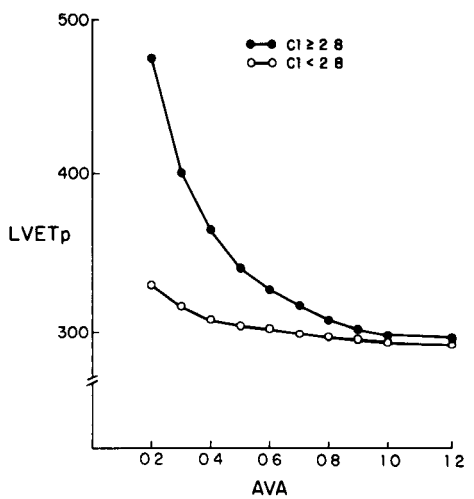
Figures 1B and C show that the difference in SV/$\sqrt{PG}$ ratios in patients with good and poor ventricular function is predominantly due to the difference in variation of stroke volume with aortic valve area For patients with good performance, SV (in milliliters) = 34.2 AVA + 50 2 (r = 0 738, $p < 0$ 01), where SV is stroke volume and AVA aortic valve area, while for those with poor function SV = 61 0 AVA + 24 7 (r = 0 673, $p < 0$ 01) On the other hand, the slopes and intercepts of linear regression equations relating pressure gradient with valve area were quite similar in the good and poor performance subgroups With good ventricular function, pressure gradiant (PG) (in mm Hg) = −56.8 AVA + 104 8 (r = −0.818, $p < 0$ 01), and with poor function, PG = −66 1 AVA + 108 0 (r = −0 495, $p < 0$ 01)

From these data, it follows that at any given aortic valve area the SV/$\sqrt{PG}$ ratio multiplied 22 5 times the reciprocal of the valve area results in a higher predicted ejection time in patients with good ventricular function (Table 1, equation 2) This is demonstrated in Figure 2, where predicted ejection time values, based on stroke volume and pressure gradient measurements and calculated valve areas, are shown over a wide range of aortic valve area for patients with good and poor ventricular function

Effect of rate correction. The theoretical effect of rate correction by the regression formula of Weissler et al (9) (Table 1, equation 3) on these predicted ejection time curves, using heart rate data derived from good and poor function subgroups, is shown in Figure 3 This demonstrates that for any aortic valve area, the predicted rate-corrected duration of ejection is significantly greater in patients with good ventricular function than in those with ventricular dysfunction

Correlation of predicted with measured ejection times. The correlation was good in all patients, with LVETp (in ms) = 1 03 LVETm − 25 (r = 0 61, $p < 0$ 001), where

Figure 2. Predicted left ventricular ejection time (LVETp in ms), on the basis of solution of the equations shown in Figure 1A as applied to the rearranged formula for aortic valve area (AVA in cm^2), for patients with good ventricular function (cardiac index [CI] ≥ 2 8, **closed circles**) and poor ventricular function (cardiac index < 2 8, **open circles**)



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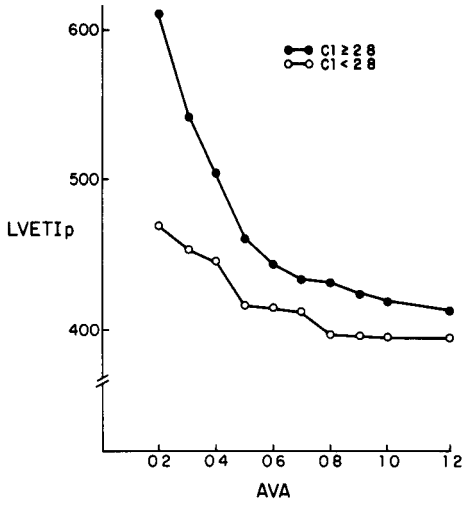

Figure 3. Rate-correction of predicted left ventricular ejection time, based on measured heart rates, demonstrates greater prolongation of left ventricular ejection time index at any aortic valve area (AVA in cm^2) among patients with good ventricular function CI = cardiac index, LVETIp = predicted left ventricular ejection time index in ms

LVETp is predicted duration of ejection and LVETm is ejection time measured at cardiac catheterization

Discussion

Relation of stroke volume and pressure gradient and ejection time in aortic stenosis. Rearrangement of the Gorlin formula (6) for calculation of aortic valve area reveals a simple solution for observed duration of ejection that, interestingly, is not directly dependent on heart rate (Table 1, equations 1 and 2) Evaluation of the hemodynamic variables that determine the duration of ejection permits both insight into the pathophysiology of pure aortic stenosis and understanding of the variability of ejection time at constant valve area.

If the relation of stroke volume and pressure gradient were to remain constant among patients with aortic stenosis, it is obvious from equation 2 that, because ejection time is inversely proportional to aortic valve area, the duration of ejection would increase in hyperbolic relation to increasing outflow obstruction. This clearly does not occur (4,5). Hemodynamic analysis demonstrates that modification of ejection time prolongation at smaller valve areas is the result of simultaneous changes in stroke volume and pressure gradient Examination of the ejection time equation reveals that reduction of the otherwise predicted increasing duration of ejection could be associated with a decrease in stroke volume, an increase in pressure gradient or a decreasing ratio involving both hemodynamic factors

Effect of ventricular function on relation of stroke volume and pressure gradient. When our patients were separated into good and poor performance subgroups on the basis of cardiac index, different strong linear correlations were found in the relation of the SV/ $\sqrt{PG}$ ratio and aortic valve area At any aortic valve area less than 1 0 cm^2, this ratio is higher in patients with good ventricular performance, and the difference between patients with good and poor ventricular performance increases as aortic obstruction increases. From the ejection time equation, it is apparent that at any valve area, the duration of ejection will be higher in patients with preserved cardiac output and will decrease as ventricular function deteriorates

It is clear from inspection of the linear regression data in Figure 1 that differences in stroke volume (SV) alone appear to explain the greater SV/ $\sqrt{PG}$ ratio in patients with good ventricular performance Even though normalization of stroke volume by the square root of individual pressure gradient (PG) markedly strengthens the correlation with aortic valve area, it is obvious from Figure 3 that mean pressure gradients within valve area groups are independent of ventricular function

Ventricular function and aortic valve area. Aortic stenosis is known to modify the relation between stroke volume and duration of ejection (9) In normal subjects, a close relation between stroke volume and ejection time was demonstrated by Weissler et al (9) In individuals with atrial fibrillation, ejection time has been shown to vary directly with the length of diastole, and thus by inference, to vary directly with stroke volume (10,11) A relation between duration of ejection and stroke volume has also been observed in subjects with aortic stenosis (9,12) However, linear correlation of ejection time with stroke volume in aortic stenosis has been weak (5,9) The present study suggests that this weaker correlation can be explained by the effects of varying cardiac index and aortic valve area in these patients

The different rates at which the SV/ $\sqrt{PG}$ ratios vary with valve area among patients with good and poor ventricular function have significantly different modifying effects on the independent inverse relation between ejection time and aortic valve area Predicted duration of ejection, calculated by solving the linear regression equations over a range of valve area from 0.2 to 1 2 cm^2 and substituting the resulting SV/ $\sqrt{PG}$ ratio values in the ejection equation is shown to increase at an accelerating rate with decreasing valve area when cardiac output is preserved (Fig 2) When ventricular function is poor, however, predicted ejection time does not significantly increase until exceedingly severe aortic obstruction is present Although the difference in predicted duration of ejection between patients with good and poor ventricular performance is small for valve areas greater than 0 8 cm^2, this difference becomes progressively larger with increasing aortic obstruction as a result of the

nonlinear effect of multiplying by the reciprocal of progressively smaller aortic valve area

Ventricular function and predicted rate-corrected ejection time. Similarly, predicted rate-corrected ejection time (Fig 3), is higher at any aortic valve area in patients with good ventricular function However, because mean cardiac index from groups of patients with aortic stenosis decreases with valve area, more patients with a smaller valve area have poor ventricular function, while more patients with less severe obstruction have good ventricular function This results in the increasing scatter of rate-corrected ejection times with decreasing valve area observed in previous studies (3–5) and explains why mean measured and rate-corrected duration of ejection need not continue to increase among groups of patients with increasing valvular obstruction

Conclusions. It is apparent that the duration of ejection in aortic stenosis is markedly dependent on ventricular performance Although ejection time is strongly determined by the SV/ $\sqrt{PG}$ ratio in any individual patient, this ratio is most dependent on changes in stroke volume (SV) that accompany ventricular dysfunction The wide range of observed ejection time in patients with severe aortic stenosis is thus a consequence of variable ventricular performance

Ventricular performance in our patients is assessed on the basis of cardiac index, a commonly used estimate of total cardiovascular function that depends on loading conditions, as well as on the contractile state of the myocardium (13,14) Thus, we recognize that cardiac performance, as measured in this study, is not equivalent to contractility Derived indexes are available that more closely approximate contractile state (15), and their evaluation may provide further insight into the mechanism of ejection time variability

Implications. Although our findings appear to discourage the use of systolic time indexes in the routine evaluation of aortic outflow obstruction, recognition of the relation of ventricular performance to the duration of ejection may have potential application Because noninvasive methods such as echocardiography (16) and radionuclide imaging (17) can provide accurate assessment of ventricular function, ejection time determination interpreted in the context of ventricular performance may result in the accurate prediction of aortic valve area Perhaps more important, discordant estimates of valve area and ejection time may be a valuable clue to left ventricular dysfunction in patients with aortic stenosis.

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